

REMARKS

Consideration of the remarks presented herein is respectfully requested. This Amendment is timely filed.

I. Amendments to the Specification and/or Claims

This amendment contains no amendments to the specification or claims.

II. Rejection of the Claims Under 35 U.S.C. §103(a)

A. GROUNDS OF REJECTION

The Examiner has rejected claims 1-54, 82, 84-85, 90, 94, 155-172, 176, 178, and 184-185 under 35 U.S.C. §103(a) as being unpatentable over Shearwater Corporation (Catalog 2001) or Vandoorne *et al.*. This rejection is respectfully traversed for the reasons provided below.

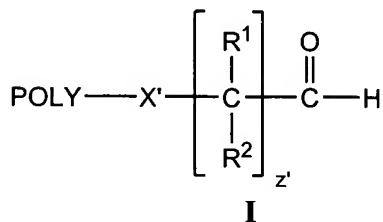
B. THE CLAIMED INVENTION

The present invention is directed to polymer alkanal reagents, and related conjugates, acetals, hydrates and hydrogels. The claimed polymer alkanal reagents are less reactive than prior art polymer aldehydes, and are therefore more selective. The polymer alkanal reagents of the invention comprise at least one aldehyde functionality coupled to a polymer segment by one or more interposing carbon atoms.

Of the claims currently under consideration by the Examiner, Claim 1 is the only independent claim. Thus, all other claims presently under consideration are either directly or indirectly dependent upon claim 1 and therefore must contain the features of claim 1.

The features of the invention, as encompassed by claim 1, are described below:

Claim 1 is directed to a water-soluble polymer having the structure:



where:

POLY is a water-soluble polymer segment;

X' is a linker moiety;

z' is an integer from 1 to about 21;

R¹, in each occurrence, is independently H or an organic radical selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, and substituted aryl;

R², in each occurrence, is independently H or an organic radical selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, and substituted aryl,

and further wherein the following apply:

-when POLY is linear:

(a) the total number of carbonyls present in said polymer is 0 or 2 or greater except when X' comprises one or more contiguous (-CH₂CH₂O-) segments,

(b) and further wherein X' is oxygen or comprises at least one (-CH₂CH₂O-) segment and z' is from 2 to 12, then at least one of R¹ or R² in at least one occurrence is an organic radical as defined above or said polymer is heterobifunctional, where POLY comprises a reactive group at one terminus that is not hydroxy, and

-when POLY is branched:

(c) either (i) at least one of R¹ or R² in at least one occurrence is an organic radical as defined above or (ii) X' includes -(CH₂CH₂O)_b- where b is from 1 to about 20 in the instance where POLY comprises a lysine residue,

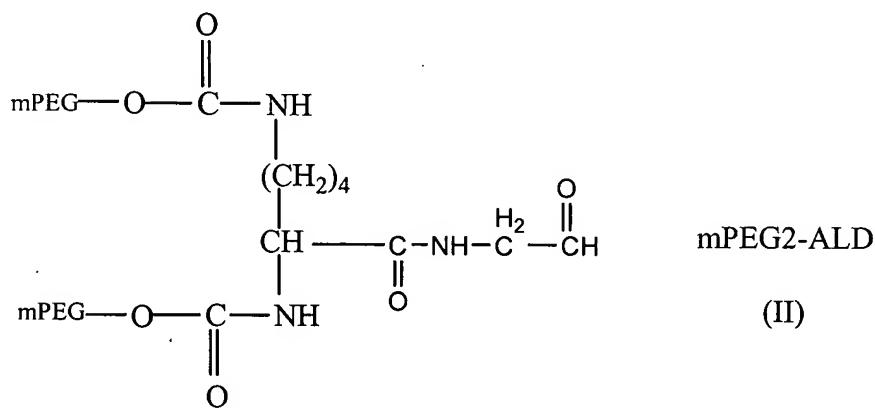
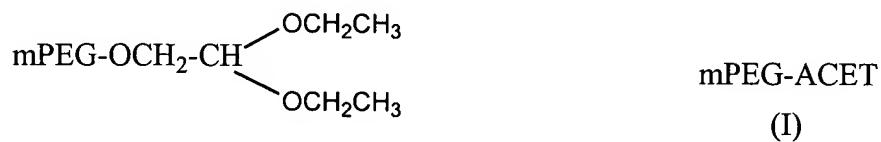
(d) and further wherein said POLY has 2 polymer arms, then neither polymer arm comprises oxygen as the only heteroatom in the instance where POLY comprises "C-H" as a branch point.

C. THE CITED ART

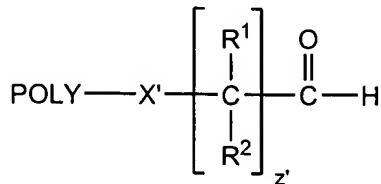
Shearwater Corporation Catalog 2001 ("Shearwater Catalog").

Shearwater Catalog lists numerous commercially available PEG derivatives and their corresponding chemical structures, in addition to describing certain facilities, the company's manufacturing capabilities, and the like.

The structures relied upon by the Examiner in the instant Office action are mPEG-acetaldehyde diethyl acetal (structure I below, "mPEG-ACET"), mPEG2-aldehyde (structure II below, "mPEG2-ALD"), and propionaldehyde (structure III below, "mPEG-ALD"), (all described on page 7 of the Shearwater Catalog).



When comparing each of the above prior art structures to the structure provided in instant claim 1, each of the recited variables has the value indicated below.



<u>Structure</u>	<u>POLY</u>	<u>X'</u>	<u>z'</u>	<u>R¹</u>	<u>R²</u>
I, linear	PEG	O	1	H	H
II. branched	PEG-2	-C(O)NH	1	H	H
III, linear	PEG	O	2	H	H

Some Differences between the Prior Art Structures and the Claimed Polymers

In considering the patentability of the instant claims over the cited art, one must consider the “wherein” language of Claim 1, which indicates additional requirements for the claimed polymers of the invention.

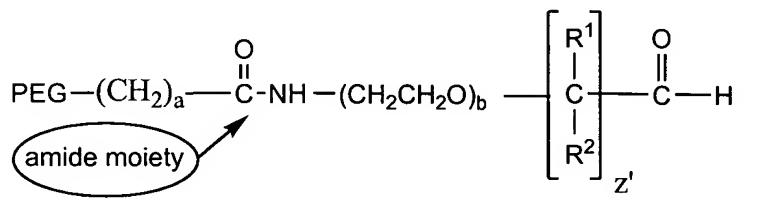
Claim 1 requires that when POLY is linear:

- (a) the total number of carbonyls present in the polymer (not counting the aldehyde carbonyl as explained on page 4, line 23, of the application) is 0 or 2 or greater except when X' comprises one or more contiguous (-CH₂CH₂O-) segments,
- (b) and further wherein X' is oxygen, or comprises at least one (-CH₂CH₂O-) segment and z' is from 2 to 12, then at least one of R¹ or R² in at least one occurrence is an organic radical as defined above or said polymer is heterobifunctional, where POLY comprises a reactive group at one terminus that is not hydroxy.

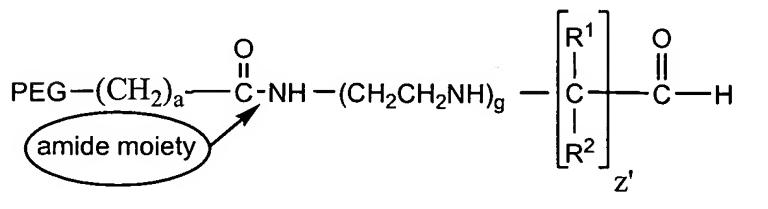
Regarding structures I and III: Although the total number of carbonyls in structures I and III is zero (when considering for the sake of argument, the aldehyde equivalent of the acetal for

structure I), and X' is oxygen, R^1 and R^2 in structures I and III are both H. However, the claimed polymers encompass a completely different type of structure, where when POLY is a linear polymer, and X' is oxygen, then at least one of R^1 or R^2 in at least one occurrence *must be an organic radical as defined in claim 1, or the polymer must be heterobifunctional*. Neither of these features is contained in either structure I or in structure III. That is to say, the carbon alpha to the acetal carbon is a primary carbon rather than a carbon substituted with an organic radical. Further, both structures I and III are mono-functional polymers rather than heterobifunctional polymers. In sum, in no way does structure I or structure III even remotely suggest an aldehyde structure of the type encompassed by claim 1, let alone read on any claim currently under consideration, due to the structural distinctions described above.

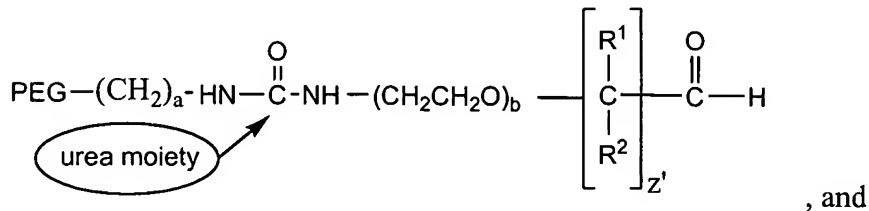
The Examiner has also asserted that structure I disclosed in the Shearwater Catalog reads on claim 167 and related claims. Claim 167 encompasses hydrate or acetal forms of the following amide or urea moiety-containing polymers:



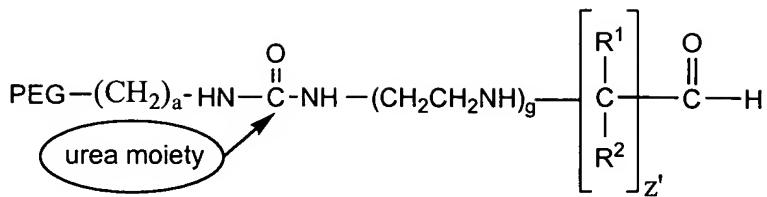
III-A



IV-A



III-C

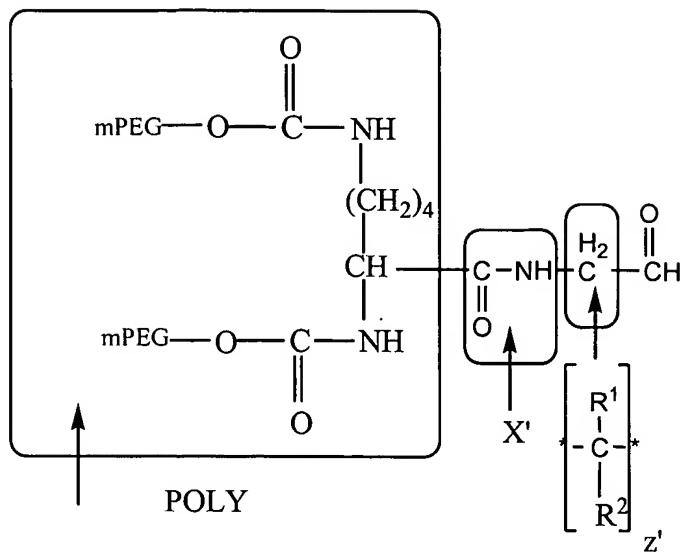


wherein PEG is poly(ethylene glycol), b and g are each independently 0 to 20, a is 0 to 6, and the remaining variables are as defined in claim 1. (For the convenience of the Examiner, amide and urea moieties have been identified in each of structures III-A, IV-A, III-C and IV-C.)

Since structure I fails to contain either an amide or a urea moiety, let alone an amide or urea moiety covalently attached to either $(-\text{CH}_2\text{CH}_2\text{O}-)_b$ or $(-\text{CH}_2\text{CH}_2\text{NH}-)_g$, in no way can structure I render obvious the polymers of claim 167 or related claims. Finally, the Shearwater Catalog as indicated provides absolutely no suggestion or motivation to modify the polymers shown therein to arrive at the polymers of the instant claims.

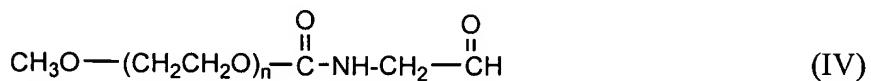
Regarding structure II: Structure II is a branched polymer where POLY comprises a lysine residue. In considering polymers encompassed by the instant invention, again, one must consider all of the limitations of the independent claim.

Claim 1 requires that when POLY is branched, either (i) at least one of R^1 or R^2 in at least one occurrence is an organic radical as defined above or (ii) X' includes $-(\text{CH}_2\text{CH}_2\text{O})_b-$ where b is from 1 to about 20 in the instance where POLY comprises a lysine residue.

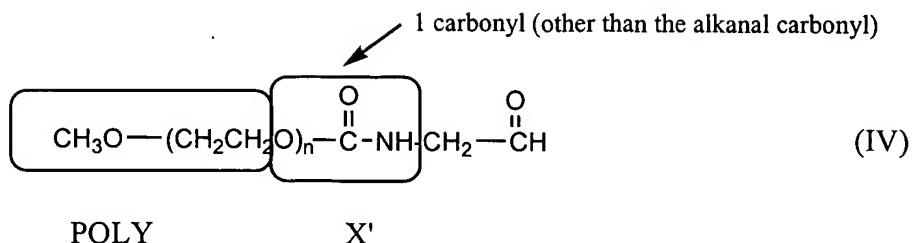


Structure II clearly falls outside of the instant claims, since neither R^1 nor R^2 is an organic radical (rather, each is H), nor does the linker X' contain the fragment $-(CH_2CH_2O)_{1-20}-$. In sum, structure II does not contain all of the elements of the recited claims. Moreover, the Shearwater Catalog contains no suggestion to modify the above structure to arrive at a polymer of the type encompassed by the Applicant's claims.

Vandoorne, et al. Vandoorne describes an improved method for converting a hydroxyl end group on PEG to an aldehyde. A reaction scheme demonstrating the method is shown on page 272 of the reference. The product, structure 6 in the reference and structure IV herein, is shown below.



Structure IV is a linear polymer. Referring to the requisite features of a polymer alkanal of the invention, as recited in claim 1, when the polymer is linear, the total number of carbonyls present in the polymer must be 0 or greater than or equal to 2, except when X' comprises one or more contiguous $(-CH_2CH_2O-)$ segments.



In examining structure IV, it can be seen that structure IV contains 1 carbonyl (other than the alkanal carbonyl). The Vandoorne structure is clearly outside the scope of the present claims, since structure IV fails to meet all of the requirements of the claims by virtue of its single non-aldehyde carbonyl group.

The method of Vandoorne relies upon the introduction of the carbonyl group into the resulting polymer, since the method requires the reaction of the starting polymer with the chloroformate reagent, 2. Vandoorne provides no suggestion to modify structure 6 therein to arrive at a polymer of the present invention. Moreover, to modify the teachings of Vandoorne to arrive at a polymer alkanal absent the additional carbonyl group would be contrary to the very teachings therein – which are directed to the use of the carbonyl-containing chloroformate reagent to produce a polymer intermediate containing an internal carbonyl group.

D. ANALYSIS

In determining whether a claimed invention is obvious, the following tenants must be adhered to:

- i. The claimed invention must be considered as a whole;
- ii. The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; and
- iii. The references must be viewed without the benefit of hindsight afforded by the claimed invention or accompanying specification.

The prior art must also teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

In considering the references relied upon by the Examiner, it can be seen that the references, when considered either singly or in combination, neither teach nor suggest all of the limitations of the Applicant's claims.

As set forth in detail in the preceding section which considers both the instant claims and the cited art, each as a whole, neither the Shearwater Catalog nor Vandoorne teach or suggest a polymer having a structure of the type encompassed by the Applicant's claims. Indeed, the structures described in each of the cited references clearly fall outside the scope of the instant claims. Further, neither of the references provides the slightest motivation to modify the structures shown therein to arrive at a polymer of the instant claims.

Since the cited art fails to teach or suggest all of the limitations of the claims under consideration, it is submitted that the claims currently pending in the application are non-obvious in view of the art of record. Withdrawal of the rejection of the claims under 35 U.S.C. §103(a) is therefore respectfully requested.

III. Conclusion

In view of the foregoing, the Applicant submits that the claims pending in the application patentably define over the cited art. A Notice of Allowance is therefore respectfully requested.

If a telephone conference would expedite the prosecution of the subject application, the Examiner is requested to call the undersigned at (650) 493-3400.

Respectfully submitted,

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